

## Patients' perspectives on the derivation and use of organoids

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### SUMMARY

Organoid research is enhancing understanding of human development and diseases as well as aiding in medication development and selection, raising hopes for even more future therapeutic options. Nevertheless, this work raises important ethical issues and there is a paucity of data regarding patients' perspectives on them. We report on 60 interviews with adult patients or parents of pediatric patients from diverse disease populations who receive medical care at a major academic research institution in the United States. Interviewees expressed broad support for organoid development and use. However, patients viewed brain organoids, and sometimes gonadal organoids, as morally distinct; and some organoid research poses moral concerns. Nonetheless, patients generally understood the potential value of such research and approved of it, provided it was aimed at good intent and conducted with ethical oversight and a robust consent process. These data should help inform conceptual and policy deliberations about appropriate organoid use.

### INTRODUCTION

Research with organoids is burgeoning across a wide range of systems. While much of this work has been at the bench, there is tremendous hope for developing therapeutic applications. Indeed, early efforts at clinical translation have been impressive, such as selecting treatments for patients with specific cystic fibrosis (CF) mutations using gut organoids (Berkers et al., 2019) and identifying medication candidates for treating Zika virus infection using brain organoids (Chen et al., 2019; Xu et al., 2016). Nevertheless, basic and translational organoid research raises important ethical and policy issues, including those related to the extent to which organoids should be permitted to mature or be used in assembloids, the provenance of the materials used to generate them, and their use in chimera research (Munsie et al., 2017). Further, depending on how organoids are used in translational research (e.g., identifying personalized treatments, transplantation, biobanking), ethical issues concerning safety, privacy, and consent will inevitably arise (Boers, et al., 2016). In addition, particular potential clinical applications necessitate specific considerations, such as the ethical acceptability of enrolling children in clinical trials involving organoids (Schneemann, et al., 2020) and the commercialization of organoid technologies (Choudhury et al., 2020).

With some exceptions, early conceptual scholarship about these issues has focused predominately on gastruloids, brain organoids, and intestinal organoids (Boers and Bredenoord, 2018; Boers, et al., 2019; Hyun, 2017). Deliberations about gastruloids have in large part interrogated their moral status and potential relationship to embryo development and questioned the appropriateness of existing regulations or

policies regarding this work (Hyun, 2017; Hyun et al., 2020a; Munsie et al., 2017; Pera et al., 2015; Pereira Daoud et al., 2020; Piotrowska, 2020). Discussions about brain organoids have engaged such issues as sentience and the ethical permissibility of pursuing advanced brain models (National Institutes of Health, 2018; Sawai et al., 2019; Hyun et al., 2020b; National Academies of Sciences, Engineering, and Medicine, 2021). Reflections on intestinal organoids have centered on their use in CF-related work (e.g., precision medicine, biobanking). Nonetheless, multiple other human organoid systems have been reported (Israeli et al., 2020; Kim et al., 2020). Consequently, broader inquiry is needed.

Furthermore, while this conceptual scholarship is valuable, the perspectives of patients, who are, after all, the sources of the tissues and recipients of potential clinical interventions, on the derivation and use of organoids are essential to informing the analysis of the ethical and policy issues. To date, two small studies in the Netherlands have been reported (Boers et al., 2018; Haselager et al., 2020). The first involved interviews with patients with CF or their parents, many of whom had participated in related organoid research. The researchers found: "(1) Respondents express a close as well as a distant relationship to organoids; (2) the open-endedness of organoid technology sparks hopes and concerns, (3) commercial use evokes cautiousness. (4) Respondents mention the importance of sound consent procedures, long-term patient engagement, responsible stewardship, and stringent conditions for commercial use" (Boers et al., 2018). The second study consisted of interviews with patients with neurologic or psychiatric diseases and members of the public regarding the derivation, use, and storage of brain organoids. In this study, interviewees broadly supported the use of brain organoids, but they





**Table 1. Demographic characteristics of interviewees (n = 60)**

<b>Gender</b>	
Male	32 (53%)
Female	28 (47%)
<b>Age (years)</b>	
<20	2 (3%)
20–29	1 (1%)
30–39	14 (23%)
40–49	7 (12%)
50–59	9 (15%)
60–69	15 (25%)
70–79	20 (9%)
<b>Race/ethnicity</b>	
Black or African American	11 (18%)
Caucasian	44 (73%)
Hispanic or Latino	1 (1%)
Asian	1 (1%)
Two or more races	3 (2%)
<b>Education level</b>	
≤ High school or GED <sup>a</sup>	6 (10%)
High school + some college	14 (23%)
College degree	19 (32%)
Graduate degree	21 (35%)
<b>Patient population</b>	
Gastrointestinal disease	10 (16%)
Neurologic condition	14 (23%)
Macular degeneration	7 (12%)
Cystic fibrosis	10 (17%)
General outpatient	19 (32%)

<sup>a</sup>General education diploma (GED) or high school equivalency certificate.

were concerned about consciousness and potential organoid misuse (Haselager et al., 2020). Together, these findings reveal that certain aspects of organoid research can be morally salient to patients and suggest there may be relatively straightforward approaches taken to manage them.

Nevertheless, there is a clear need for data from patients from other settings and who face other diseases and conditions where organoid research is playing a critical role in advancing scientific understanding and holds clinical translation potential. To gather these data we interviewed

patients from diverse disease populations who receive medical care at a major academic research institution in the United States.

## RESULTS

A total of 60 patients or their parents were interviewed. Their demographic characteristics are summarized in Table 1. Here we report on six broad, and sometimes inter-related, themes that emerged: (1) there is broad support for the derivation and use of organoids; (2) brain organoids are inherently different from other organoids; (3) certain research poses concern; (4) a sense of personal connection to organoids does not correspond with a desire for control over their use; (5) a variety of background influences and experiences shape views about organoids; and (6) there are factors associated with acceptable use (good intent, oversight, consent). Our analysis did not identify any substantial differences among interviewees based on their demographic characteristics or disease group. Consequently, results are reported in aggregate, but attributions for particular quotations include participant identification number, gender (F, female; M, male), and patient population; second cohort interviews that included expanded domains are marked with asterisks. Representative quotations are provided in the text and additional examples in Table 2.

### Broad support for the derivation and use of organoids

All interviewees supported the derivation and use of a wide array of organoids and across a range of potential uses (Table 2). Interviewees were enthusiastic about the potential for organoids to advance medical science, enable therapeutic “breakthroughs,” and provide hope for future treatments and improved health.

I think it can be very helpful in the future. It’s awesome how the scientists can have come up with something like this, to help anybody, basically, who needs them. I think it’s a very brave and very bold move, to future science, to help others. (I37\*, M, general outpatient)

### Uses of organoids

Interviewees endorsed numerous uses for organoids, including general research, drug development and testing, personalized treatments, and transplantation. Some connected the potential benefits of organoid research to their personal health, although not necessarily to the condition for which they were recruited. Others’ excitement centered on possible benefits to family and friends suffering from significant health challenges as well as the potential to alleviate suffering and improve health for humankind.

I would say, you know, this is marvelous. I can’t think of anything that really could come close to it, and I can



**Table 2. Exemplary quotes by theme**

**Theme 1: broad support for the derivation and use of organoids**

Derivation of different types of organoids	I think as long as they all have a functional purpose in either helping or discovering new things for people they all make sense. I wouldn't limit it to only certain types of organs, because they'll all probably have a practical use for one person or another. (I15, F, CF)
Uses of organoids	I'm not a scientist, so I don't know a lot about the science, but anything that, any technique, research that can be done to address the kind of issues that we're discussing in here, curing diseases, treatments, I mean, I think of the COVID situation where they're fighting desperately to find vaccines and treatments. I mean, any additions to the toolkit, any new tool in the toolkit to help find cures and treat patients with these- well, with any kind of disorder, but I'm obviously familiar with cystic fibrosis and I told you my sister has multiple myeloma. I mean, it just- we all know people that have chronic disorders, whether its cancer or whatever. I think it's very exciting. Very exciting. (I18, M, parent of a child with CF)
As a research tool	I think it's pretty neat. I think the whole idea with stem cells and just being able to do things in vitro outside the body that can ultimately improve what medicine can do and I guess just kind of create some additional potential cures for diseases and things like that, it's a starting point, and I think it's something that absolutely needs to be done. (I5, M, general outpatient)

**Theme 2: brain organoids are inherently different than other organoids**

Sentience	I don't know that it alarms me...what would a full-blown brain look like? Like would it be able to think? Would it be replicate how I think or you think or is it just, you know, because all those synapse fires, and misfires, and non-fires. You know, many of them are based on experience, or you know, it doesn't mean that I, you know, if you put my brain, you know, whatever it is, the organoid— [interviewee's name] organoid brain into Bob the Cat, then he wouldn't know not to put his hand in the fire or whatever. (I55*, M, neurologic condition)
Brain as the locus of personhood	I think I do actually have a little hesitation there. I think the brain controls who you are as a person. The heart or lungs don't, so that I'm totally ok with. The brain, I do feel a little bit different about it. (I43*, F, general outpatient)
Brain as the body's "command center"	I feel like, for me, I feel like [a brain's] different. I think of a brain—as the brain as like the umbrella. And the heart and everything else is like hanging. Maybe like the brain is the tree and everything else is the hanging fruit. (I58*, F, general outpatient)

**Theme 3: certain research poses concern**

Eugenic purposes	Again, if it's not like we're trying to create the perfect- <laughs> the perfect race like Adolf Hitler...then it doesn't bother me. (I18, male, parent of child with CF)
Creating a living independent entity	As long as we do it in a way that avoids sort of the God syndrome, where I become so smart I've decided I'm going to develop a new form of life or something. You know, so I think that's almost- that's Isaac Asimov science fiction—but that would be part of that notion of a barrier where you don't want to go.(I39*, M, macular degeneration)
Tampering with natural processes	As far as I'm concerned, you know, the real abuse of this as I would see it would be to actually extend an individual's life past their natural life expectancy. Now, I'm getting into almost science fiction. -it's like a forest fire. The forest fire clears out all the old undergrowth. Makes room for new growth, and that is what death is in some ways. Everybody goes through a life cycle, and if somebody tries to- you know, to extend life a little bit, that's fine, but you know, if you try to extend life indefinitely, that's where I see massive issues. (I52*, M, macular degeneration)



**Theme 4: a sense of personal connection to organoids does not correspond with a desire for control over their use**

Limited sense of connection /desire for information about use	<b>Interviewer:</b> Do you feel a relationship to those, are those your parts, little bits of you that are in these Petri dishes or are they just a bunch of cells... <b>Interviewee:</b> Mainly ... a bunch of cells, I mean there might be some type of connection there but not that deep of a connection...but down the road I would like to know what happened, if I donated cells to build a liver let's say. (I8, M, gastrointestinal disease)
Sense of connection/comfortable with broad use	I view [cells donated for organoid research] as a part of me, but if I give my permission for [them] to be used, then it would be okay. (I35*, F, general outpatient)

**Theme 5: views about organoids are shaped by a variety of background influences and experiences**

Family health challenges/pro-science world view	My son has type 1 diabetes, so we have dealt with that and he, you know, is a guy who loves to scream about how unfair it is that his pancreas doesn't work and things like that. So I'm, you know, I'm a 100 percent pro-science guy. I don't have ethical qualms about stem cells or embryonic stem cells or anything like that. I think if scientists can figure out ways to make people healthier and able to live more productive lives then I'm all for it. (I4, M, general outpatient)
Professional experience/pro-science world view	<b>Interviewer:</b> Is there anything that you think kind of guides your views on [organoids]? <b>Interviewee:</b> I mean, I'm not really religious. I would consider myself more spiritual, but I work in the STEM field. I am- you know, I support science. (I34*, F, general outpatient)
Pro-science/pro-research world view	I think science guides my beliefs a lot. And that's why I'm all for the research being done. (I57*, F, neurologic condition)
Religion	Well, I was more concerned about everyone having to be of a genius standing...of humans interfering too much in what God has planned for us, or given to us. (I2, F, macular degeneration)

**Theme 6: factors associated with acceptable use**

Derivation and use of brain organoids	I think it depends on the motive, the goals, the what it is they're trying to accomplish with [brain organoids], what they're trying to, again, create, create something or someone who I am not then I would be very concerned about that. I would be very worried about that. But if they're trying to get more information about how the brain works, I would be fully supportive of that. (I41*, F, neurologic condition)
Connecting multiple organoids together	As long as it fits into the quality of life, or life and death, or medical reasoning, I don't believe there's a limit to what you should be able to connect. But that red line is fishing, or experimenting for the sake of experimenting for profit's sake. (I30*, M, general outpatient)
Types of researchers	<b>Interviewer:</b> What are your thoughts about the researchers that are doing this? <b>Interviewee:</b> When it comes to the academics and someone like NIH that's government, but they're still tied in with a lot of academia, I would probably feel more comfortable with them, knowing usually what the purpose is or usually is: to help. But the pharmaceutical companies, yes, I'd have a little bit more concerns because of the profit part. (I56*, F, general outpatient)

imagine what it could do for just like my own problem with macular degeneration, that—what that could do to really help things. (I2, F, macular degeneration)

A few interviewees described advantages of organoids as research tools. For example, one believed organoid models would allow scientists to research organ-specific therapies outside of the human body, thereby avoiding potential risk to human research subjects. Another

viewed organoid models as a preferable alternative to animal research.

I'm excited about it, because I think it allows scientists to make greater discoveries without affecting live patients. They can do some incredible things with organoids that they wouldn't dare do with a living creature ... so it's not destructive testing to the human or animals. (I9, M, gastrointestinal disease)



### Types of organoids

Interviewees reflected upon the acceptability of various organoid models, including stomach, intestine, liver, thyroid, lung, retina, brain, and, in later interviews, ovaries and testes. There was broad support for all organoid types presented. A few interviewees expressed increased interest in a specific type of organoid for personal reasons.

All I think are wonderful. I guess personally, I have a sister-in-law who's quadriplegic, so the nerve one is especially interesting. (I12, F, gastrointestinal disease)

However, some interviewees were hesitant about particular types of organoids, most commonly, gonadal and brain organoids. While some were concerned about the potential for gonadal organoids to create “lab babies” and perpetual egg and sperm donors, brain organoids, as described below, raised special concerns for the majority of interviewees.

### Brain organoids are inherently different from other organoids

Many patients viewed brain organoids as inherently different from other organoid types. Underlying this difference were questions about sentience and the perception that the brain was the locus of personhood (see Table 2).

I think scientifically [the brain]'s the same as other organoids. But empirically, to me, my brain is what makes me. (I57\*, F, neurologic condition)

While interviewees expressed hesitation about brain organoids, this did not preclude their support for their derivation and use.

I think there's a big line drawn ... between all the other organs and then the brain ... I'm not saying that I don't think you should develop brain organoids. I think it's actually probably a good thing. (I14, M, parent of a child with CF)

When explicitly asked, patients supported a range of specific uses for brain organoids, including identifying treatment for neurologic conditions (e.g., Alzheimer disease), personalized medicine (e.g., selecting medications for psychiatric conditions), studying infectious diseases (e.g., HIV or Zika virus), tissue transplantation (e.g., into areas affected by stroke or injury), and general research.

Interviewee: [The] brain is another one of the organs that, although a lot of research has been done studying the brain, there's a lot more that can be done, specifically in regards to some conditions like Alzheimer's. So I think it's—I think it's great, yes, I do.

Interviewer: How about for identifying treatments—like psychiatric treatments, personalized treatments. Psychiatric conditions like schizophrenia or, I don't know, bipolar depression. I mean, if they were using little mini-

brains to perhaps identify and then treat that, do you think that's okay?

Interviewee: I do, especially because the mini-brains are, you know, they are mini-brains, so you would be able to do a lot of your testing on that mini-brain, in a sense to see how they might react to different procedures or medications versus using a person. So I think using the mini-brain to try to reach those—to get those results is great.

Interviewer: Okay. And how about if scientists could grow ... brain tissue and then implant it into someone's brain to improve—or what do you think about that? How does that strike you?

Interviewee: I told you, once again, it's amazing! I mean, that's what science is all about, becoming better at treating all kinds of factors that affect human beings physically, mentally, emotionally, whatever. (I46\*, M, general outpatient)

### Certain research poses concern

Despite widespread support for the derivation and use of organoids, patients also described uses that posed concern. These included creating “life” (and the pursuit of other “ungodly” purposes), developing mature brain organoids, connecting multiple organoids together (a.k.a. “connectoids”), and commercialization.

#### Creating “life” and the pursuit of other “ungodly” purposes

Although such uses were not discussed in the informational presentation at the outset of the interviews, patients voiced opposition to research designed to create an independently living entity.

Interviewer: Okay. Can you think of any unacceptable uses for an organoid or organoid research?

Interviewee: Recognizing organoids are tiny and simple, but if at any point somebody decided to build, like, Frankenstein's monster out of them. Basically create a full being. (I20, M, neurologic condition)

Others raised concerns about other “ungodly” purposes (e.g., uses that interfered with natural processes, such as creating a new species, enabling humans to live forever, and eugenics).

Interviewer: What do you think about ... the creation of brain or cerebral organoids to test medications or to study how brain diseases, things like Alzheimer's?





Interviewee: I think that would be highly acceptable as long as it was very well controlled so that you wouldn't have people—extreme, extremophiles—getting into it and using the research to create things that I would consider, quote, "ungodly." (I28, F, gastrointestinal disease)

#### *Developing mature brain organoids*

For some, developing mature brain organoids raised concern, particularly the possibility of "full" brain transplants.

What constitutes a fully functioning brain? I don't know. I mean, I think of that Frankenstein movie where they have the little brain in the glass, and I don't know what that means, but I guess I would draw the line there. I would be opposed to that, because this is where I don't know how you separate the brain from the human, and if you can use it to help people who have brain damage or have epilepsy or things like this where you can fix parts of the brain that are damaged, then that's great, but, I mean, seriously to do a brain transplant? Is that going to be the person? (I26, F, macular degeneration)

#### *Connectoids*

Some interviewees were uncomfortable with researchers connecting multiple organoids together, especially if one of the organoids being connected was a brain organoid.

Connecting the brain just seems like perhaps that's going too far, because then it makes me think of them as real living things, and that makes me worry about how they'd be treated or what would happen to them or would they have a quality of life or something like that. (I45\*, F, general outpatient)

Interviewees' discomfort with fully mature brain organoids and connectoids appeared to be triggered by the sense that these activities edged closer to creating "life."

#### *Commercialization*

Most interviewees believed commercialization of organoids was inevitable—"everything is commercial" (I52\*, M, macular degeneration); however, approximately half expressed unease with commercialization. For some, this discomfort was rooted in a belief that commercialization would result in exorbitantly priced therapeutics that could be cost prohibitive and further exacerbate existing health care inequities.

I would have a concern about organoids at some point being developed and commercialized and the benefits are only available for the rich. (I6, M, gastrointestinal disease)

Others were wary of researchers working for commercial entities like "Big Pharma." These individuals believed that industry researchers' ethics could be corrupted by profit-driven motives.

#### **A sense of personal connection to organoids does not correspond with a desire for control over their use**

The majority of interviewees reported no special connection or relationship to organoids derived from their cells, regardless of organoid type. Many viewed organoids as a cluster of cells or "spare parts." Several of those who held this opinion viewed the donation of cells for organoid research as similar to organ donation.

My nature is not a kidney. The kidney doesn't have its own mind or anything from my experience, so I have no problem with the cells actually being coaxed into an organ. And if people can be healed by that process, no problem. People donate organs as it is, now, for transplant purposes, so what's the difference? (I52\*, M, macular degeneration)

However, a minority of interviewees indicated they would feel a connection to organoids derived from their cells. Those who shared this view believed organoids retained unique donor characteristics and therefore perceived organoids derived from their cells as a little piece of themselves.

Interviewer: If you donated these cells, and scientists were creating little mini [name] hearts and brains and eyes and such, do you feel like those are yours? Are they part of you? They're little extensions of you, or are you like, no, those are a bunch of cells, that's not me?

Interviewee: I would just think they were a small part of me.

Interviewer: Do you feel a little bit of ownership over them? Can you explain to me how you feel?

Interviewee: No, I wouldn't feel any ownership. I would just think, okay, they're my cells. It's a part of me somewhere out here. (I50\*, F, general outpatient)

For some interviewees, a sense of connection depended on the type of organoid. A few who described organoids developed from their cells as "spare parts" described feeling more of a connection with brain and/or gonadal organoids than other types of organoids since they contained more of their individual essence.

Interviewer: Do you feel those are yours, like you have a relationship with them, or are they just cells?

Interviewee: No, I think they're just cells. I wouldn't feel like they're mine, like a connection to them, no.



Interviewer: Except for the brain? Do you feel differently about the brain?

Interviewee: Yes, I do. I do feel differently about the brain and also perhaps ovaries, like sex organs. (I45\*, F, general outpatient)

Views about interviewees' relationship to organoids did not always correspond with a desire for control over how their cells were used in organoid research. Some of those who viewed organoids as clusters of cells expressed a desire for information about, or control over, how their cells were used (see [Table 2](#)).

Interviewer: What do you think? Do you see [organoids] as little parts of you?

Interviewee: No ... [but] I want to know what it's going to be used for. I'd like to be informed of the—of what's happened with them. (I23, M, neurologic condition)

On the other hand, some who described feeling a connection to their organoids were comfortable surrendering control over the use of their cells. In several instances, interviewees attributed their permissive attitude to feeling a lack of "ownership" over their cells.

Oh, I think those cells would carry forward a part of me or, you know, but I don't necessarily retain ownership. Just like when we have children, those children will always be a part of us, but we don't own them and control them. You know, they're their own free human beings. I think if our cells are used for good purposes, we don't retain ownership. (I9, M, gastrointestinal disease)

### Views about organoids are shaped by a variety of background influences and experiences

Perhaps not surprisingly, in our interviews support for organoid research was shaped by a variety of background influences and experiences. Patients cited a myriad of such influences, including a strong sense of altruism, a pro-science/pro-research worldview, religious/spiritual values, experiences (e.g., professional experience, exposure to other cultures), personal and/or family health challenges, and an interest in/exposure to science fiction. Of note, references to science fiction arose spontaneously in approximately half of all interviews, including those across all demographic groups.

Interviewer: What do you think about organoids in general?

Interviewee: It's great. I'm a lifelong science fiction buff. So, I assume that eventually medicine is going to grow us replacement parts. (I44\*, M, neurologic condition)

Finally, despite the fact that the majority of patients expressed strong altruistic sentiments, when asked whether they believed patients had a duty to participate in research that ultimately improves medical care, the overwhelming majority answered no.

I wouldn't say "duty" ... because I don't think duty would be the answer, the correct answer, because I think someone should still have a choice. (I56\*, F, general outpatient)

### Factors associated with acceptable use

Finally, we identified three factors that appear to be associated with support for use: good intent, oversight, and consent.

#### Good intent

Good intent was a cross-cutting theme undergirding the acceptability of the derivation of a range of organoid types, research uses supported, and the extent to which organoids should be permitted to develop and/or connect to other organoids. In addition, operating with good intent facilitated trust in the different types of researchers working with organoids (i.e., academic, commercial, governmental), as well as the commercialization of organoids (See [Table 2](#)).

As long as [commercialization]'s to create new medicines for treatments, that would be fine with me. (I1, F, macular degeneration)

#### Oversight

The role of oversight was raised by some interviewees as a mechanism for preventing unacceptable use of organoids, enhancing trust in both the research being conducted and the types of researchers working with organoids.

Be my guest and take my cells and do organoid research. I've given you permission to now own them, but, as I said, I would like to know that there's protocols and rules here. (I6, M, gastrointestinal disease)

#### Consent

Informed consent was viewed by many as the mechanism for exercising autonomy, promoting transparency, defining limits of acceptable use, and fostering trust in the research and researchers.

I think if people can specify how or what they want it to not be used for that you would get more participants, because you'll draw in a broader spectrum of donors because you'll get the people who will say "I don't care what you do. I'm totally detached from it." You'll get the people who say "Well, I'm fine with this or that." So I like the idea of saying "You can use it for"—you got your little boxes there, and you can check off all the boxes ... you know whose is what and going forward—but at least the donor has a sense of control. They feel in control about what happens with the material that leaves their body. (I26, F, macular degeneration).



## DISCUSSION

Our study provides the first systematic data regarding perspectives on the derivation and use of organoids, from patients who receive medical care at a major academic research institution in the United States. These data reveal broad support for the derivation of all organoid types, for a wide range of uses among patients with a variety of diseases and conditions.

Our research expands upon the findings of two small interview studies from the Netherlands described above (Boers et al., 2018; Haselager et al., 2020). First, our study included patients from a variety of disease groups as well as primary care outpatients. Second, our interviewees come from a drastically different health care system. Third, we discussed a variety of uses for all organoid types, enabling us to elicit views regarding organoid research in general, as well as studies that are type and/or use specific. Fourth, with one exception, none of our interviewees had participated in organoid research that offered personal benefit, removing a potential source of bias. Fifth, interviewees were provided with a presentation about organoid research at the outset of the interview.

We found areas of concordance and discordance between our data and those previously described. In particular, we also found broad support for the derivation and use of organoids in research and concerns about commercialization (Boers et al., 2018). However, our interviewees were concerned about profit-driven motives and this concern was not unique to organoids. In addition, while our interviewees echoed strong altruistic sentiments regarding organoid research (Boers et al., 2018; Haselager et al., 2020), they did not endorse an ethical duty to participate in research (Haselager et al., 2020). Finally, unlike the interviews with adults and parents of children with CF conducted in the Netherlands, where participants' concerns gradually arose during the course of the conversation (Haselager et al., 2020), our interviewees tended to become more comfortable with organoid research as the discussion progressed and questions were asked and answered.

Nevertheless, our interviewees clearly viewed brain organoids, and sometimes gonadal organoids, as morally distinct from other organoid types. Some of these concerns reflect discussions described in conceptual literature regarding "consciousness" (Sawai et al., 2019; Hyun et al., 2020b; Lavazza and Pizzetti, 2020), while others involved nuanced associations with what it means to be human. Perhaps surprisingly, despite such concerns, patients generally understood the potential value of such research and approved of it, provided it was motivated by good intent and conducted with ethics oversight and a robust consent process.

These empirical findings may both challenge and support aspects of the recently issued International Society

for Stem Cell Research (ISSCR) *Guidelines for Stem Cell Research and Clinical Translation*. Specifically, under these guidelines, *in vitro* organoid research is categorized as being exempt from "a specialized scientific and ethics oversight process after being assessed by the appropriate existing mandates and committees for laboratory research" (International Society for Stem Cell Research, 2021, p. 10). This categorization was based on the observation that, "At this time, there is no biological evidence to suggest any issues of concern, such as consciousness or pain perception with organoids corresponding to CNS tissues, that would warrant review through the specialized oversight process" (International Society for Stem Cell Research, 2021, p. 10). While this scientific justification is clear, the uses of biological materials in organoid research must be consistent with the donors' consent, and routine research oversight is still needed. Yet, this approach may incompletely account for patients' views about organoid research and support for it, which is predicated upon appropriate oversight and consent. Similarly, given the moral salience of particular types of organoids and organoid research to patients, treating all organoid research as the same may be inadequate. Further empirical work will be needed to assess the acceptability of these practices for patients.

Our findings also highlight the need for having accurate information about organoids available. However, doing so can and will be challenging. For example, even though we provided a scientifically accurate presentation about organoids at the outset of our interviews, at some point during the interviews many participants used analogies to science fiction in articulating their perspectives, a phenomenon also reported by the team in the Netherlands. While this did not dampen interviewees' enthusiasm for pursuing work with organoids, it is uncertain if this would be the case for those who simply hear about reports of this work in the media or otherwise. Establishing and maintaining trust in organoid research will likely be predicated upon proper communication and understanding of it. Accordingly, and consistent with the ISSCR guidelines (see Recommendation 4.1), efforts should be taken to create and disseminate accurate information about organoids that can be used not only when obtaining informed consent for this research, but also for the general public (International Society for Stem Cell Research, 2021).

As a related matter, even though potential clinical applications of organoid research are quite promising, at present it is obviously critical to recognize the nascent status of the science. However, many of our interviewee's enthusiasm about the research and its possibilities exceeds the current reality (Marsoner et al., 2018; Xinaris, 2019). Accordingly, when recruiting participants for research, especially projects involving clinical translation, it will be important that the current state of the science is understood to avoid





problems with therapeutic misconception whereby participants inflate the likely therapeutic value of an experimental intervention (Hornig and Grady, 2003). Ensuring this understanding will require far more than the inclusion of a couple of sentences in an informed consent document.

Despite the value of the information we obtained, this study has several potential limitations that should be considered when interpreting our findings. First, our patient population was predominantly Caucasian, was highly educated, and had been able to access care at a single academic research institution. As such, we cannot rule out the possibility that broad support for derivation and use of organoids hinges on these factors. Accordingly, it is essential that future work be conducted at other institutions and in different geographic locations across the globe, with an emphasis on engaging those of multiple races and ethnicities as well as educational backgrounds. Second, the interviews were conducted during the COVID-19 pandemic. As such, perspectives on cutting-edge research may have played a role in responses to organoid research. Finally, as with all qualitative research, while our findings provide rich information from a relatively small number of participants, they cannot be quantified or generalized to other populations and contexts. Similarly, these data are intended to be hypothesis generating rather than testing. Future quantitative research, such as large national surveys with representative study populations, would be needed to address such issues.

In conclusion, our findings suggest that patients are generally supportive of current uses of organoids, provided that they are well-intended and have appropriate oversight and informed consent. These data suggest that explicit consent for potential research and clinical uses should be obtained. In addition, investigators would be wise to anticipate the need to educate potential participants about organoid research to avoid misperceptions (and even leaps into science fiction) that can easily happen when discussing organoids. In sum, it is our hope that these data will serve to inform conceptual and policy deliberations about the acceptable uses of organoids, especially in regard to brain and gonadal embryoids, as well as complex connectoids and assembloids, which raised concern in our interviews. Finally, we hope that these data will better position researchers, policy makers, and those charged with ethics and regulatory oversight of research to help ensure that the approaches used are ethically sound.

## EXPERIMENTAL PROCEDURES

We conducted semi-structured interviews with patients with a selected range of diseases and conditions as well as primary care outpatients. The Johns Hopkins Medicine Institutional Review Board approved this research (IRB00222993).

Interviews were conducted between March 2020 and December 2020 by two members of the research team (J.M.B., E.M.) with extensive qualitative research experience. Interviews were conducted by Zoom videoconferencing or phone, depending on participant preference. After obtaining oral consent, an informational presentation about organoids was provided. Once technical questions about the presentation were answered, interviews proceeded according to a guide. Interviews lasted approximately 1 h and were audio-recorded. Patients were offered \$50 for their participation by direct payment or a gift card. Additional information about the experimental procedures is provided in the [Supplement](#).

## SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/10.1016/j.stemcr.2021.07.004>.

## AUTHOR CONTRIBUTIONS

J.B.: conception and design, collection and/or assembly of data, data analysis and interpretation, manuscript writing, final approval of manuscript. E.M.: conception and design, administrative support, collection and/or assembly of data, data analysis and interpretation, final approval of manuscript. D.M.: conception and design, data analysis and interpretation, final approval of manuscript. M.D.: conception and design, financial support, provision of study material or patients, data analysis and interpretation, final approval of manuscript. J.S.: conception and design, financial support, data analysis and interpretation, manuscript writing, final approval of manuscript.

## CONFLICTS OF INTEREST

Jeremy Sugarman is a member of Merck KGaA's Bioethics Advisory Panel and Stem Cell Research Oversight Committee, a member of IQVIA's Ethics Advisory Panel, a member of Aspen Neurosciences Scientific Advisory Board, a member of a Merck data monitoring committee, a consultant to Biogen, and a consultant to Portola Pharmaceuticals, Inc. None of these activities are related to the material discussed in this article. No other authors have outside interests to declare.

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